REMARKS

Applicants thank the Examiner for entering Claim 9 into the record. Claim 73 is currently amended and claims 74, 75 and 79 remain the same as those in last correspondence. Applicants respectfully request reconsideration of the claims in the current format and Applicants believe that the currently amended claims are in condition for allowance.

Information Disclosure Statement

Paper No. 2 in the Information Disclosure Statement is attached herein. Applicants respectfully request the Examiner to consider the claims in light of the aforementioned reference Paper No. 2.

Objections Withdrawn

Applicants acknowledge with appreciation the objections withdrawn regarding the oath/declaration, claims 74 and 75 for reciting the phrases "said plant is tomato" and "said plant is potato" in light of the amendments thereto, and claims 73-75 for double patenting in light of the terminal disclaimer filed on 3-1-2004.

Claim Rejections Maintained

Double Patenting

The rejection of claim 73 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-5 of U.S. Patent No. 5,612,487 was maintained for

lack of a terminal disclaimer. A terminal disclaimer to that effect is included in this communication to obviate the instant rejection.

35 USC § 102

The Examiner rejected claims 73-74 and 79 under 35 U.S.C. 102(b) as anticipated by Goodman et al. (WO 87/00865 – IDS-2). The Examiner contends that a given protein's immunological properties are inherent in nature and that the physiologically active proteins as disclosed in Goodman et al. are the same as those antigenic proteins disclosed in the instant invention. Furthermore, the Examiner contends that the instant claims are directed to antigens that elicit all immune responses.

Although not conceding to the Examiner's rejection, Applicants have amended claim 73 to clearly indicate that the vaccines as disclosed in the instant invention are intended to elicit production of antibodies that are specific to the plant-produced antigens. It is not Applicants' intention that the claims are to encompass all immune responses.

As to the Examiner's contention that a given protein's immunological properties are inherent in nature, Applicants respectfully disagree. It is well known in the pertinent art that a protein will react differently with a certain polyclonal antibody depending on the state of the protein (i.e. denatured or native) and the posttranslational modifications accorded to the nascent polypeptide. As an example, different epitopes would form with the introduction of varying number of oligosaccharides to hemagglutinin of influenza A/H3N2 virus (Abe et al., Effect of the Addition of Oligosaccharides on the Biological Activities and Antigenicity of Influenza A/H3N2 Virus Hemagglutinin. *J. Virol.* (2004) 78(18): 9605-11). Applicants respectfully remind the

Examiner that a protein's immunological properties are determined not just by the epitopes present in the polypeptide, but also by its posttranslational modifications and its tertiary structure.

Applicants contend claim 73 as amended is distinguishable from Goodman et al. in that the instant claims relate to viral antigens for vaccine as opposed to the physiologically active mammalian proteins in the Goodman reference. Although the Goodman reference discusses the transgenic plant production of viral antigen proteins from leukemia and lymphotrophic retroviruses, herpes simplex virus, hepatitis B virus and adenovirus, the cited reference merely contemplates the production of these proteins in their physiologically active state. Nowhere in the Goodman reference is found a disclosure relating to the use of these viral antigen proteins as constituents in a vaccine. In fact, many of the viral antigen proteins serve a distinct function in the proliferation of the viral particle and the interaction between the virus and the host cell. For example, the Simian virus 40 large T antigen interacts with the tumor suppressor p53 and the transcriptional coactivators CBP and p300 in the regulation of cell proliferation and tumerogenesis (Poulin et al., p53 targets Simian virus 40 large T antigen for acetylation by CBP. *J. Virol.* (2004) 78(15): 8245-53). Many of these viral antigen proteins were discovered through immunoscreening and were named as such for lack of a known function when first discovered. The mere tag of *antigen* to the name of the protein should not be misinterpreted in such a way as to indicate that particular protein is only serving to be an antigen. It is in this context that the viral antigens disclosed in the cited reference should be viewed. The Goodman reference contemplates the transgenic plant production of a host of mammalian proteins, including some viral antigen proteins, in their physiologically active state. These proteins are not disclosed to constitute a vaccine, which distinguishes from the instant claims.

Merriam-Webster Online dictionary defines "physiological" as "characteristic of or appropriate to an organism's health or normal functioning" www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=physiological&x=14y=14. Additionally, "physiological activity" is typically synonymous with the words "biological activity." And the biological activity of a given protein can be maintained when the antigenicity of the same protein is changed. To evade the antibody pressures of the host cells, the influenza A/H3N2 virus changes the antigenicity of hemagglutinin by adding new oligosaccharides to the polypeptide without changing its biological activity (Abe et al., supra). It is therefore evident that a physiologically active protein as disclosed in the Goodman reference is different from a antigen protein disclosed in this invention for the purpose of making a vaccine.

Applicant's view about the Goodman reference is bolstered by a decision by the Board of Patent Appeals and Interferences (*Ex parte* Roy Curtis III and Guy A. Cardineau, Appeal No. 93-4341, Heard January 11, 1996). The Board explicitly stated that the Goodman reference does not teach a transgenic plant which expresses an antigenic protein, and said protein induces an immune response in animals. It is apparent that the Board viewed the Goodman reference as teaching a transgenic plant to function as mini-factory for the production of mammalian proteins, the function of which does not extend to the area of eliciting immune responses in animals. The Board held:

> Where the product can have a physiological effect on ingestion, Goodman discloses, it may be sufficient that the product be retained within the plant. This will be true where the plant part is edible. See Goodman, paragraph bridging pages 9 and 10. However, Goodman does not disclose or suggest retaining in the plant a protein which has no effect on ingestion. Like all of the references discussed above, **Goodman does not disclose or suggest a transgenic plant which (a) expresses a DNA sequence coding for a coloniozation antigen or antigenic determinant thereof, or Streptococcus mutans of Escherichia coli, and (b) induces a secretory iummune response**. (emphasis added)

Because the proteins disclosed in the instant invention and the cited reference can be distinguished structurally and functionally, it cannot be said that the cited reference anticipates the instant claims, which relates to a method of producing a vaccine.

Goodman also only exemplifies the dicot, tobacco to support its disclosures. Monocots are not exemplified. This ultimately resulted in the claims being limited to dicots. For this and other reasons, therefore, the rejection under 35 U.S.C. 102(b) should be withdrawn.

The Examiner also rejected claims 73-74 and 79 under 35 U.S.C. 102(e) as anticipated by Goodman et al. (U.S. Patent 4,956,282 – IDS-2). The examiner contends: 1. The Goodman reference disclose the expression of the same proteins by the same methods as the instant claims, said proteins would have the same immunological properties as those of the instant claims. 2. The Goodman reference specifically discusses the use of transgenic plants to express recombinant viral antigen proteins from leukemia and lymphotrophic retroviruses, herpes simplex virus, hepatitis B virus and adenovirus. The Examiner acknowledged that the expressed digestive proteins in Goodman may or may not have immunogenic activity. 3. The rejected claims are not limited to the production of antibodies with specificity for the protein, but encompass all immune responses. 4. The rejected claims are drawn to a method of conferring immunity.

With regard to Point 1, Applicants respectfully remind the Examiner that a protein's physiological activity and antigenicity do not coincide. It is apparent from the above hemagglutinin example that a protein may retain its biological activity while changing its antigenicity. The Goodman reference discusses a method to produce biologically active proteins. These proteins can be harvested from transgenic plants immediately after translation without

sacrificing their biological activity. For viral antigen production in plants for the purpose of producing a vaccine, the proteins need to be sufficiently modified after translation to mimic the native antigen. Therefore the instant claims disclose viral antigens that may have dramatically different immunological properties from the proteins disclosed in the Goodman reference even when the molecular constructs are similar.

As to Point 2, the Examiner is reminded that name alone does not reflect the purpose and nature of the protein disclosed in the cited reference and the instant claims. The viral antigen proteins serve a variety of physiological functions. They were named as antigens merely because of a lack of better description when they were first discovered through immunoscreening. For example, a large surface antigen of the hepatitis B virus serves as a regulator of intracellular trafficking (Walters et al., Superinfection exclusion in duck hepatitis B virus infection is mediated by the large surface antigen. *J. Virol.* (2004) 78: 7925-37). The intended purpose of producing physiologically active proteins is fundamentally different from the purpose of the instant claims, i.e. producing viral antigens as vaccine. The Examiner seemed to concede that the proteins disclosed in the Goodman reference may or may not have immunogenic activity.

With respect to Point 3, Applicants have amended Claim 73 to limit the claims to the production of antibodies with the specificity for the viral antigen produced in transgenic plants. Applicants do not intend to claim that the viral vaccine produced in transgenic plants would elicit immune responses of all kinds.

With respect to Point 4, it is clear from the instant amended claims that they are drawn to a method of producing a vaccine in plants, but not a method of conferring immunity to either plants or animals. The state of the art at the time of filing of the Goodman reference was such that oral vaccine was not contemplated to be feasible of being produced in plants (See Service,

Science (1994) 263: 1522-1524). A clear copy of the reference is presented herewith for the Examiner's review.

Based on the foregoing, it is apparent that the instant amended claims are patentably distinguishable from the cited reference. The rejection under 35 U.S.C. 102(b) should be withdrawn.

35 U.S.C. 103

The Examiner rejected claim 75 under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (WO 87/00865 – IDS-2). The Examiner maintains that the use of potato plants is an obvious variation of the method disclosed in the cited reference. Applicants wish to remind the Examiner that the rejected claim is a dependent claim, which should be examined in view of the limitations provided in the pertinent independent claim (claim 73). Applicants agree with the Examiner that tomato and potato belong to the same phylogenic family (*Solanaciai*). The language of claim 75, "The method of claim 73 wherein said plant is a potato plant", clearly incorporates all the limitations in claim 73 into claim 75. Because claim 73 is patentably distinguishable from the cited reference, the use of potato plants for the method of producing a vaccine cannot be said to be an obvious variation from the method of the cited reference which teaches the production of physiologically active proteins in plants.

The Examiner also rejected claim 75 under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (U.S. Patent 4,956,282 – IDS-2). The Examiner cited the same reasons for rejection as in the previous obviousness rejection. Again the Examiner is reminded that the instant claim is a dependent claim which incorporates all the limitations in the pertinent independent claim. As such, the use of potato plants for the production of vaccines cannot be

said to be an obvious variation from the method disclosed in the cited reference wherein the potato plants are used for the production of physiologically active mammalian proteins including certain proteins labeled viral antigen proteins.

35 U.S.C. 112

The Examiner rejected claims 73-75 and 79 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as invention. Applicants acknowledge with appreciation the Examiner's advice and have amended claim 73 to clearly point out and distinctly claim the subject invention. In so doing, Applicants are careful in not introducing any new matter into the amended claim, while heeding the Examiner's advice.

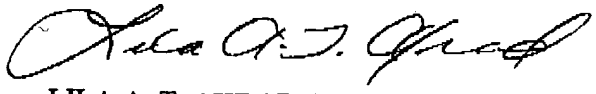
Applicants respectfully request that the Examiner withdraw this rejection.

CONCLUSION

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a response in the above identified application for one month from September 2, 2004 to October 2, 2004. Applicant is a small entity, therefore, please charge Deposit Account Number 26-0084 in the amount of $55.00 for one month to cover the cost of the extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



LILA A. T. AKRAD, Registration No. 52,550
McKee, Voorhees & Sease, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
CUSTOMER NO: 22885

-pw-

Attorneys of Record